

**APPENDIX** (*clean claims*)**CLEAN SET OF AMENDED CLAIMS**

1. **(currently amended):** A method for making a prognosis in a subject of (i) enhanced recovery from an inflammatory condition, or (ii) increased at risk of developing, the inflammatory condition,  
the method comprising determining a genotype defined by one or more polymorphic sites in the toll-like receptor 2 (TLR-2) nucleic acid sequence in the subject, wherein said genotype is (a) a protective genotype that is predictive or indicative of an enhanced ability of the subject to recover from the inflammatory condition, or (b) a risk genotype that is predictive or indicative of said increased risk for developing the inflammatory condition.
  
2. **(currently amended):** The method of claim 1, wherein the one or more polymorphic sites includes position 201 of SEQ ID NO: 1 or a polymorphic site in linkage disequilibrium therewith.
  
3. **(currently amended):** The method of claim 1, further comprising comparing the determined genotype with genotypes that are known to be prognostic for recovery from an inflammatory condition.
  
4. **(currently amended):** The method of claim 1, further comprising ascertaining the TLR-2 sequence of the subject.
  
5. **(currently amended):** The method of claim 1, wherein said genotype determination is performed on a nucleic acid sample from the subject.
  
6. **(currently amended):** The method of claim 5, further comprising the step of obtaining the nucleic acid sample from the subject .
  
7. **(currently amended):** The method of claim 1, wherein said genotype is determined by one or more of the following methods:
  - (a) restriction fragment length analysis;
  - (b) sequencing;
  - (c) hybridization;
  - (d) oligonucleotide ligation assay;
  - (e) ligation rolling circle amplification;
  - (f) 5' nuclease assay;
  - (g) polymerase proofreading methods;
  - (h) allele specific PCR; and
  - (i) reading sequence data.

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8. *(currently amended)*: The method of claim 1, wherein the risk genotype of the subject is predictive or indicative of (a) decreased likelihood of recovery from the inflammatory condition or (b) increased risk of having a poor outcome from the inflammatory condition.

9. *(currently amended)*: The method of claim 8, wherein the subject is critically ill and the presence of the risk genotype is predictive or indicative of severe cardiovascular or respiratory dysfunction.

10. *(currently amended)*: The method of claim 8, wherein the risk genotype comprises at least one T nucleotide at position 201 of SEQ ID NO:1.

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12. *(currently amended)*: The method of claim 1, wherein the subject is critically ill and the protective genotype is predictive or indicative of less severe cardiovascular or respiratory dysfunction.

13. *(currently amended)*: The method of claim 1, wherein the protective genotype is defined as homozygosity for the A nucleotide at position 201 of SEQ ID NO: 1.

14. *(currently amended)*: The method of claim 1, wherein the inflammatory condition is one that is due to, or associated with: Gram-positive, Gram-negative, culture-negative or fungal sepsis; septicemia; septic shock; fever; bacterial viral, fungal or parasitic infection including Group A streptococcus infection; inflammation due to trauma, surgery or a medical or surgical condition associated with increased risk of infection or sepsis; pneumonia; systemic inflammatory response syndrome (SIRS); Acute Respiratory Distress Syndrome (ARDS); acute lung injury; pancreatitis; bacteremia, including meningococcemia; peritonitis; bowel infection; abdominal abscess; surgery; chronic inflammatory disease; ischemia; tissue damage due to (i) disease, (ii) chemotherapy (iii) radiotherapy, or a reaction to an ingested, inhaled, infused, injected, or delivered substance; glomerulonephritis; an opportunistic infection; kidney failure and dialysis; immunosuppressive therapy; immunocompromise; endocarditis; cystic fibrosis; diabetes mellitus; chronic renal failure; bronchiectasis; chronic obstructive pulmonary disease (COPD); chronic bronchitis; emphysema; post-pump syndrome; cardiac stun syndrome; myocardial infarction; stroke; congestive heart failure; hepatitis; cirrhosis; epiglottitis; gas gangrene; toxic shock syndrome; mycobacterial tuberculosis; *Pneumocystic carinii* pneumonia; Leishmaniasis; hemolytic uremic syndrome; Dengue hemorrhagic fever; pelvic inflammatory disease; Legionella; Lyme disease; Influenza A; Epstein-Barr virus; encephalitis; autoimmunity and inflammation due to rheumatoid arthritis, osteoarthritis, or systemic lupus erythematosus; inflammatory bowel disease, idiopathic pulmonary fibrosis, sarcoidosis, hypersensitivity pneumonitis, systemic vasculitis, Wegener's granulomatosis; an organ or tissue transplant and/or transplant rejection; graft-versus-host disease; sickle cell anemia; nephrotic syndrome; or toxicity caused by monoclonal antibody or cytokine therapy.

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**15. (currently amended):** The method of claim 14, wherein the inflammatory condition is SIRS.

**16. (currently amended):** A method of identifying a polymorphism in a TLR-2 sequence that correlates with or is associated with prognosis of recovery from an inflammatory condition in a subject, the method comprising:

- (a) obtaining TLR-2 sequence information from a plurality of subjects with an inflammatory condition;
- (b) based on the sequence information of (a), identifying at least one site of polymorphism in the TLR-2 sequence ;
- (c) determining genotypes defined by said at least one polymorphism for individual subjects;
- (d) determining recovery ability of individual subjects from the inflammatory condition; and
- (e) correlating the genotypes determined in step (c) with the subjects' recovery abilities determined in step (d),

thereby identifying said polymorphisms in said TLR-2 sequence .

**17. (currently amended):** The method of claim 16, wherein the inflammatory condition is one that is due to, or associated with: Gram-positive, Gram-negative, culture-negative or fungal sepsis; septicemia; septic shock; fever; bacterial viral, fungal or parasitic infection including Group A streptococcus infection; inflammation due to trauma, surgery or a medical or surgical condition associated with increased risk of infection or sepsis; pneumonia; systemic inflammatory response syndrome (SIRS); Acute Respiratory Distress Syndrome (ARDS); acute lung injury;; pancreatitis; bacteremia including meningococcemia; peritonitis; bowel infection; abdominal abscess;; surgery; chronic inflammatory disease; ischemia; tissue damage due to (i) disease, (ii) chemotherapy (iii) radiotherapy, or a reaction to an ingested, inhaled, infused, injected, or delivered substance; glomerulonephritis; an opportunistic infection; kidney failure and dialysis; immunosuppressive therapy; immunocompromise; endocarditis; cystic fibrosis; diabetes mellitus; chronic renal failure; bronchiectasis; chronic obstructive pulmonary disease (COPD); chronic bronchitis; emphysema; post-pump syndrome; cardiac stun syndrome; myocardial infarction; stroke; congestive heart failure; hepatitis; cirrhosis; epiglottitis; gas gangrene; toxic shock syndrome; mycobacterial tuberculosis; *Pneumocystic carinii* pneumonia; Leishmaniasis; hemolytic uremic syndrome; Dengue hemorrhagic fever; pelvic inflammatory disease; Legionella; Lyme disease; Influenza A; Epstein-Barr virus; encephalitis; autoimmunity and inflammation due to rheumatoid arthritis, osteoarthritis, or systemic lupus erythematosus; inflammatory bowel disease, idiopathic pulmonary fibrosis, sarcoidosis, hypersensitivity pneumonitis, systemic vasculitis, Wegener's granulomatosis; an organ or tissue transplant and/or transplant rejection; graft-versus-host disease; sickle cell anemia; nephrotic syndrome; or toxicity caused by monoclonal antibody or cytokine therapy.

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**18. (currently amended):** A kit useful for determining a genotype of a subject or subjects at a defined polymorphic nucleotide position in a TLR-sequence from the subject or subjects, which genotype is associated with a prognosis of the subject's ability to recover from an inflammatory condition, the kit comprising;

- (a) a restriction enzyme with specificity that distinguishes alternate nucleotides at the polymorphic site or sites; or
- (b) a labeled oligonucleotide having sufficient complementarity to an alternate nucleotide sequence at the polymorphic site such that the oligonucleotide hybridizes in a distinguishable manner to a sequence that comprises said alternate nucleotide sequence, thereby permitting determination of the genotype at the polymorphic site; and
- (c) optionally, instructions for use of said enzyme and/or said oligonucleotides in determining the genotype.

**19. (currently amended):** The kit of claim 18, wherein the polymorphic site is at nucleotide position 201 of SEQ ID NO:1.

**20. (currently amended):** The kit of claim 18 further comprising an oligonucleotide primer or a set of oligonucleotides suitable to amplify a region flanking the polymorphic site.

**21. (currently amended):** The kit of claim 20, further comprising a polymerization agent that promotes or permits nucleotide polymerization.

**22. (currently amended):** A method for identifying subjects as being suitable for a trial that tests efficacy of a candidate drug known to be, or suspected of being, useful for treating an inflammatory disease or condition, the method comprising

- (a) determining a genotype defined by one or more polymorphic sites in the TLR-2 sequence for each of said subjects, wherein said genotype is indicative of the subject's recovery ability from the inflammatory disease or condition, and
- (b) sorting subjects into a suitable and unsuitable group for said trial based on the subjects' genotype.

**23. (currently amended):** A method for testing a candidate drug for its efficacy in the treatment of an inflammatory disease or condition wherein said disease or condition is associated with a genotype defined by a polymorphism in a TLR-2 gene, comprising:

- (a) identifying subjects that are suitable for a trial that tests said candidate drug in accordance with of claim 22 ; and

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(b) administering the candidate drug to each of said subjects, and comparing the subjects' responses to said candidate drug in comparison with the subjects' genotype,  
thereby testing said candidate drug.

**24. (currently amended):** The method of claim 23, wherein a subject's response to the candidate drug is measured as the ability to recover from the inflammatory condition.

**25. (currently amended):** The method of claim 22 wherein the inflammatory disease or condition is associated with a gram positive infection.

**26. (currently amended):** The method of claim 23 wherein the inflammatory disease or condition is associated with a gram positive infection.

**27. (currently amended):** The method of claim 24 method of claim 1 wherein the inflammatory condition is a result of a gram positive infection wherein if said genotype is a risk genotype, it is indicative of the subject's risk of gram positive infection.

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**40. (currently amended):** The method of claim 1 wherein the inflammatory condition is a result of a gram positive infection, wherein if said genotype is a risk genotype, it is indicative of the subject's risk of gram positive infection.

**41. (original):** The method of claim 40, wherein the polymorphic site is at position 201 of SEQ ID NO:1.

**42. (currently amended):** The method of claim 40, further comprising ascertaining the TLR-2 gene sequence of the subject.

**43. (currently amended):** The method of claim 40,, wherein said genotype determination is performed on a nucleic acid sample from the subject.

**44. (currently amended):** The method of claim 43, further comprising the step of obtaining the nucleic acid sample from the subject.

**45. (currently amended):** The method of claim 40, wherein said genotype is determined by one or more of the following techniques:

- (a) restriction fragment length analysis;
- (b) sequencing;
- (c) hybridization;
- (d) oligonucleotide ligation assay;

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- (e) ligation rolling circle amplification;
- (f) 5' nuclease assay;
- (g) polymerase proofreading methods;
- (h) allele specific PCR; and
- (i) reading sequence data.

**46. (currently amended):** The method of claim 40, wherein the risk genotype of the subject is predictive or indicative of the subject's risk of developing a gram positive infection.

**47. (original):** The method of claim 46, wherein the risk genotype has at least one A nucleotide at position 201 of SEQ ID NO: 1.

**48. (currently amended):** The method of claim 46, wherein the protective genotype is defined as homozygosity for T at position 201 of SEQ ID NO:1.

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**52. (currently amended):** An array of nucleic acid molecules immobilized to a solid support, the array comprising:

- (a) a first set of oligonucleotides that
  - (i) hybridize to a nucleic acid molecule consisting of SEQ ID NO:1 in which the nucleotide at position 201 is A, under conditions wherein
  - (ii) the oligonucleotides of the first set do not substantially hybridize to a nucleic acid molecule consisting of SEQ ID NO:1 in which the nucleotide at position 201 is T; and/or
- (b) a second set of oligonucleotides that
  - (i) hybridize to a nucleic acid molecule consisting of SEQ ID NO: 1, in which the nucleotide at position 201 is T, under conditions wherein
  - (ii) the oligonucleotides of the second set will not substantially hybridize to a nucleic acid molecule consisting of SEQ ID NO: 1 in which the nucleotide at position 201 is A.

**Cancel Claims 53-55**